Relapsing yersinia infection

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Infection with *Yersinia enterocolitica* usually results in a benign and self limiting enteric illness with or without mesenteric lymphadenopathy.[1] Diagnosis is made by direct culture of yersinia from stools, and in immunocompetent adults there is said to be a rapid and measurable serological response.[2] If necessary the illness can usually be cured by treatment with tetracyclines, co-trimoxazole, or trimethoprim.[3] The case that we report did not conform to this pattern.

Case report

A 29 year old woman presented with a two week history of abdominal pain, diarrhoea, and vomiting. She had a fever (39°C) and mild tenderness in the left iliac fossa. She had a white cell count of $26{\cdot}1\times10^9$/l (neutrophils 90%) and a C reactive protein concentration of 46 mg/l (normal <8). Culture of stool, blood, and urine yielded negative results. A small bowel enema showed thickened folds of terminal ileum, but a rectal biopsy specimen was normal. She improved spontaneously over the course of a week.

She presented again one month later with diarrhoea, abdominal pain, weight loss, malaise, generalised lymphadenopathy, and an abdominal mass. Sigmoidoscopy and barium enema yielded normal findings. Rubbery lymph nodes in the small bowel mesentery and mesocolon consistent with lymphoma were found at laparotomy, but histological examination showed a necrotising granulomatous lymphadenitis typical of yersinia infection. Culture of pus from the lymph nodes was negative for yersinia, but methods specific to yersinia were not used. Repeated faecal cultures were negative and serum immunoglobulin concentrations were normal. She improved with two months' treatment with tetracycline 2 g daily, but two months after stopping this she relapsed. Colonoscopic biopsy specimens showed mild inflammatory changes, especially in the sigmoid colon, but were negative on culture for yersinia. Despite a prolonged second course of tetracycline she relapsed three months after it was withdrawn. She had similar clinical and laboratory abnormalities to those seen previously but also had a normochromic anaemia (haemoglobin concentration 90 g/l). Her condition remitted during four months' treatment with co-trimoxazole 0·96 g twice daily, but the drug was stopped when she became pregnant. By the third trimester she had again relapsed and she had symptoms until she had a normal child at 32 weeks' gestation.

She rapidly improved while taking co-trimoxazole, which was maintained for six months, but again relapsed when it was withdrawn. Barium follow through showed multiple thickened folds in the distal and terminal ileum. Stool cultures remained negative, and antibodies to *Y enterocolitica* serotypes 0:3, 0:5, 0:6, 0:8, and 0:9 were absent. Indirect immunofluorescence testing of the original lymph node blocks yielded a positive result with a polyvalent rabbit antiserum specific against serotypes 0:3, 0:5, 0:8, and 0:9 and with a polyclonal rabbit antiserum specific against the plasmid encoded outer membrane of *Y enterocolitica*.[4] The bacilli were localised between the lymphocytes. She was treated with ciprofloxacin 1 g daily for four weeks and her condition remitted immediately. She remained well three years later.

Comment

Reports of chronic yersinia infection are scant.[1] This patient undoubtedly had symptomatic colitis and histological evidence of this disease nine months after her initial illness and remained ill for two and a half years afterwards. Two other features of this case were unusual. Firstly, stool cultures and antibody titres specific to yersinia were consistently negative and the diagnosis made only by using an indirect immunofluorescence test for *Y enterocolitica* in biopsy material. This novel method has shown that as many as 62% of patients with the systemic form of yersinia infection have negative faecal cultures and titres of agglutinins.[4] The true incidence of yersinia enteritis is therefore probably underestimated. In addition, serotype 0:8 may be associated with more severe extramesenteric forms of the disease than the more familiar serotypes 0:3 and 0:9. Secondly, the patient responded well and promptly to tetracycline and co-trimoxazole but relapsed repeatedly after their withdrawal. These drugs occasionally fail in this condition,[3] but the usual pattern is failure to respond at all rather than relapse on their withdrawal. The reported 100% efficacy of ciprofloxacin[3] may be related to the high intracellular concentrations achieved with this antibiotic.

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Safety of intramuscular injection of hepatitis B vaccine in haemophiliacs

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People with haemophilia are at risk of developing hepatitis B from the injection of contaminated concentrates of clotting factor. It is generally recommended that they should be immunised against the virus. Injections of hepatitis B vaccine are usually given intramuscularly into the upper arm. Intramuscular injections, however, are generally considered to be contraindicated in haemophiliacs, some authorities stating that they should not be given in any circumstances. As a result hepatitis B vaccine has been given to haemophiliacs by subcutaneous[1-3] or intravenous[4] injection. We report our experience of giving intramuscular injections of hepatitis B vaccine to haemophiliacs.

Patients, methods, and results

We gave hepatitis B vaccine (H-B-Vax, Merck Sharp and Dohme) to 51 children attending our haemophilia centre (table). The dose, as recommended by the manufacturers, was 0·5 ml (10 μg) for children aged less than 10 years and 1·0 ml (20 μg) for the others. Each child received a course of three injections. Thirty

Numbers of children with haemophilia or von Willebrand's disease given hepatitis B vaccine by severity of disease and by age

Condition	Age ≤10 years	Age >10 years	Total
Haemophilia A:			
Severe*	15	9	24
Moderate or mild†	7	3	10
Haemophilia B:			
Severe*	2	1	3
Moderate or mild†	3‡	1	4
Von Willebrand's disease:			
Girls	3	3	6
Boys	2	2	4

*Clotting factor concentration ≤10 U/l.
†Clotting factor concentration >10 U/l.
‡Includes one girl with symptoms.

eight were immunised in the upper arm, 10 in the buttock, and three in the thigh. The injection was given with a 23 gauge needle. Whenever possible pressure was applied to the vaccination site for one to two minutes after the injection.

Six of the 153 injections (4%) resulted in bruising, none severe enough to warrant an injection of concentrate. Three children had repeated attacks of vomiting, which began a few hours after the first dose in two and two days after the third dose in the third. One child had a febrile illness with myalgia two days after the third dose of vaccine. There were no other reactions. We did not routinely measure titres of hepatitis B antibody.

Comment

The manufacturer's data sheet for hepatitis B vaccine has always stated that the vaccine is for intramuscular use only and should not be given intravenously, subcutaneously, or intradermally. We therefore decided to give it by intramuscular injection. Others have given the vaccine subcutaneously[1-3] or intravenously[4] because of the theoretical risk of bleeding. No differences were reported between haemophiliacs given subcutaneous[1-3] or intravenous[4] injections and normal controls. Of the 11 haemophiliacs who responded to a questionnaire in a study by Janco,[2] two (18%) complained of soreness or swelling at the site of injection. In a series of 1083 homosexual men injected intramuscularly the incidence of sore arms was 15·8%.[5] The incidence of bruising in our series was lower (4%). The difference may be due to the fact that in the other series the incidence of side effects was estimated by means of a questionnaire whereas in our series it was established by routine questions at follow up visits. Furthermore, we studied only children, who would perhaps be unlikely to complain to their parents about sore arms for fear of a further injection. None was needed—an important fact at a time of anxiety about the safety of clotting factor concentrates. The point we wish to make, however, is that there were no serious bruises and no treatment was needed for haematoma induced by intramuscular injection.

The low incidence of side effects is probably due to several factors, including the type of material injected, its volume, and the size of the needle. Other products may not prove to be as free from the risk of causing bruising. Our experience shows that intramuscular injections are no longer completely contraindicated in haemophiliacs.

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Increasing suicide rates among young men in England and Wales

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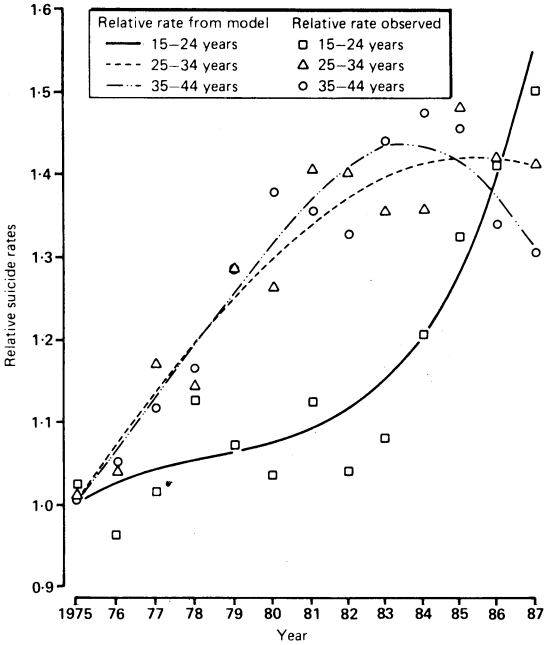
We recently reported an analysis of routinely collected suicide statistics that showed a sharp increase in the suicide rate among young people in Leicestershire.[1] In view of the interest this finding generated,[2] we extended our analysis to cover England and Wales and to investigate age specific and sex specific trends in greater depth.

Methods and results

Numbers of suicides by age and sex and by age and sex specific base populations were obtained from routine data from the Office of Population Censuses and Surveys for 1975-87.[3] Stratum specific suicide rates were treated as having a Poisson distribution. A multiplicative regression model was created with the generalised interactive modelling (GLIM) 3·77 program[4] to investigate temporal changes in the underlying rate of suicide within each age and sex stratum. Age was coded as a seven level categorical factor (15-24 years=1, 25-34=2, ... 65-74=6, 75-84=7) and time was represented by YEAR, a continuous covariate taking values between 0 and 12 (0=1975, 1=1976, ... 12=1987). The model was given parameters such that the age-sex interaction terms estimated stratum specific suicide rates in 1975 and the age-sex-time interactions estimated the manner in which these rates had changed over time. The time changes were found



Relative suicide rates by age and year in young males, England and Wales, 1975-87 (fitted age specific rates in 1975 are defined as 1·0)